

(1) If tissue cells are brought from their liquid culture medium, after several washings, into a medium free from electrolytes, then within a few seconds the following phenomena, consisting of three main effects, take place: (a) an assumption of globular form by the cells; (b) the appearance of a vivid Brownian movement of the granules and vacuoles in the cytoplasm, as a sign of a maximal reduction of the viscosity in consequence of a discharge with simultaneous increasing absorption of water; (c) a process of slow coagulation in the cytoplasm, which manifests itself in the appearance of new particles in vivid Brownian movement, which continuously increase in size. The gradual multiplication and increase of the particles is best seen with dark field illumination, but the vivid Brownian movement is also well seen with direct illumination.

(2) In some of the cells which have become globular, there occurs a bursting of the cell, with extrusion of liquid contents containing particles in Brownian movement (analogous to hypotonic hæmolysis with extrusion of hæmoglobin). Sometimes the torn parts adhere together again after diminution of the interior pressure.

(3) The presence of non-electrolytes in the medium ( $n/36-n/12$  dextrose:  $n/5-n/1$  urea) does not hinder the appearance of the phenomena described, but naturally reduces the activity of the Brownian movement in the cytoplasm.

(4) The phenomena described are reversible. The reversal can be produced after several minutes by means of Ringer solution,  $n/10$  sodium chloride, or  $n/10$  sodium bromide. The cells regain their former shape extremely quickly, with immediate stoppage of the Brownian movement in the cytoplasm. The cells then show normal vital staining.

(5) The phenomena can only be produced with living and not with dead cells. Failure is a sure sign of cell death.

The results of these experiments prove the justness of the above assumptions. Furthermore, they show that hypotonic hæmolysis is only a special case of a general phenomenon in tissue cells. They reveal, furthermore, a fundamental property of tissue cells in which the salt ions of the tissue liquid participate decisively in the maintenance of the particle charge of the protoplasm.

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### A Syndrome produced by Diverse Nocuous Agents

EXPERIMENTS on rats show that if the organism is severely damaged by acute non-specific nocuous agents such as exposure to cold, surgical injury, production of spinal shock (transsection of the cord), excessive muscular exercise, or intoxications with sublethal doses of diverse drugs (adrenaline, atropine, morphine, formaldehyde, etc.), a typical syndrome appears, the symptoms of which are independent of the nature of the damaging agent or the pharmacological type of the drug employed, and represent rather a response to damage as such.

This syndrome develops in three stages: during the first stage, 6-48 hours after the initial injury, one observes rapid decrease in size of the thymus, spleen, lymph glands and liver; disappearance of fat tissue; cedema formation, especially in the thymus and loose retroperitoneal connective tissue; accumulation of pleural and peritoneal transudate; loss of muscular

tone; fall of body temperature; formation of acute erosions in the digestive tract, particularly in the stomach, small intestine and appendix; loss of cortical lipoids and chromaffin substance from the adrenals; and sometimes hyperæmia of the skin, exophthalmos, increased lachrymation and salivation. In particularly severe cases, focal necrosis of the liver and dense clouding of the crystalline lens are observed.

In the second stage, beginning 48 hours after the injury, the adrenals are greatly enlarged but regain their lipoid granules, while the medullary chromaffin cells show vacuolization; the cedema begins to disappear; numerous basophiles appear in the pituitary; the thyroid shows a tendency towards hyperplasia (more marked in the guinea pig); general body growth ceases and the gonads become atrophic; in lactating animals, milk secretion stops. It would seem that the anterior pituitary ceases production of growth and gonadotropic hormones and prolactin in favour of increased elaboration of thyrotropic and adrenotropic principles, which may be regarded as more urgently needed in such emergencies.

If the treatment be continued with relatively small doses of the drug or relatively slight injuries, the animals will build up such resistance that in the later part of the second stage the appearance and function of their organs returns practically to normal; but with further continued treatment, after a period of one to three months (depending on the severity of the damaging agent), the animals lose their resistance and succumb with symptoms similar to those seen in the first stage, this phase of exhaustion being regarded as the third stage of the syndrome.

We consider the first stage to be the expression of a general alarm of the organism when suddenly confronted with a critical situation, and therefore term it the 'general alarm reaction'. Since the syndrome as a whole seems to represent a generalised effort of the organism to adapt itself to new conditions, it might be termed the 'general adaptation syndrome'. It might be compared to other general defence reactions such as inflammation or the formation of immune bodies. The symptoms of the alarm reaction are very similar to those of histamine toxicosis or of surgical or anaphylactic shock; it is therefore not unlikely that an essential part in the initiation of the syndrome is the liberation of large quantities of histamine or some similar substance, which may be released from the tissues either mechanically in surgical injury, or by other means in other cases. It seems to us that more or less pronounced forms of this three-stage reaction represent the usual response of the organism to stimuli such as temperature changes, drugs, muscular exercise, etc., to which habituation or inurement can occur.

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May 18.

### Estimation of Fatty Acids in Organic Mixtures

For the determination of the volatile fatty acids in cheese, it is usual to subject the acidified cheese mush to a normal steam distillation at constant volume. In this laboratory, it is the custom to collect a volume of distillate equal to three times the volume of the liquid in the distillation flask, and